

## **Description of Additional Supplementary Files**

### **Supplementary Movie 1. Architecture and gating mechanism of *Drosophila* Slo**

Slo comprises a transmembrane domain (TMD) and a domain-swapped intracellular gating ring composed of two RCK domains. The TMD consists of a selectivity filter embedded in a pore domain and a voltage sensor domain. Upon  $\text{Ca}^{2+}$ -binding, the RCK1 N-lobe moves outwards and pulls helix S6 of the TMD along. This leads to an expansion of the central cavity adjacent to the selectivity filter and activation of  $\text{K}^+$  translocation.

### **Supplementary Movie 2. Predicted drug-binding pockets on the *Drosophila* Slo surface**

Several potential binding pockets for small molecules were predicted in the gating ring and the transmembrane domain of Slo. These pockets offer the potential to design compounds binding to them that might lock Slo in either the open or the closed conformation.

### **Supplementary Movie 3. Verruculogen binding**

Verruculogen binds to the previously identified S6 pocket and locks the transmembrane domain in the inactive conformation.

### **Supplementary Movie 4. Emodepside binding**

Emodepside binds to the central cavity and serves as an additional ring below the selectivity filter.